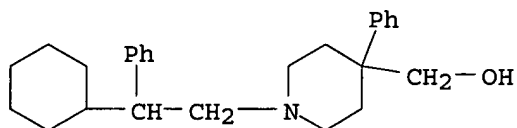
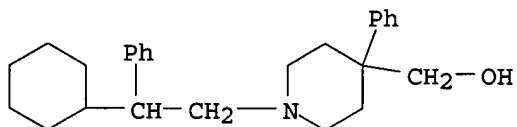


RN 96763-96-1 CAPLUS

CN 4-Piperidinemethanol, 1-(β -cyclohexylphenethyl)-4-phenyl-,
hydrochloride (7CI) (CA INDEX NAME)

● HCl

RN 804442-77-1 CAPLUS

CN 4-Piperidinemethanol, 1-(2-cyclohexyl-2-phenylethyl)-4-phenyl- (9CI) (CA
INDEX NAME)

L11 ANSWER 49 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

GI For diagram(s), see printed CA Issue.

AB The title derivs., of general formula (I), in which R was CH₂OH, CH(OH)Me, or CH-(OH)Et, A represented a C1 to C6 alkylidene radical, and R' was an alkoxy, a substituted-alkoxy, an aryloxy, an aralkoxy an aryl, an heterocyclic, or a tetrahydrofurfuryloxy radical, were prepared by either the reduction of an appropriate derivative of I (R = an alkoxy carbonyl radical, Ac, or EtCO and A and R' as stated) or the alkylation of a piperidine of general formula (I, AR' = H) (II) [R = CH₂OH, CH(OH)Me, or CH(OH)Et] with an halide of type R'AX (III) (X = I, Br, or Cl and R' and A as stated). Thus, 8 parts I (R = CO₂Et, A = CH₂CH₂ R' = 2-tetrahydrofurfuryloxy in 120 parts Et₂O added to 1 part LiAlH₄ in 120 parts Et₂O, the suspension boiled 10 min., cooled, and treated with 75 parts Rochelle salt (as 20% aqueous soln.), the mixture extracted with Et₂O, and the Et₂O extract evaporated and disd. gave

I (R = CH₂OH, A = CH₂CH₂, R' = 2-tetrahydrofurfuryloxy, b0.05 160°, n₂₀D 1.5303. Similarly prepared were the following I (R, A, R', and m.p. given): CH₂OH, CH₂CH₂CH₂CH₂, EtO (b0.4 155°, n₂₀D 1.5180), -; CH₂OH, CH₂, 2-tetrahydrofuryl, 78-80°; CH₂OH, CH₂CH₂, morpholino, 130°; CH₂OH, CH₂CH₂, piperidino, 106°; CH₂OH, CH₂CH₂,

PhOCH₂CH₂O, 78°; CH₂OH, CH₂CH₂, PhCH₂O, 82-4°. Na (10 parts) added in two portions to 10 parts I (R = CO₂Et, A = CH₂CH₂, R' = EtO) in 35 parts EtOH, the solution boiled 30 min., cooled, diluted with H₂O (10 vols.), extracted (exhaustively) with Et₂O, and the dried Et₂O exts. distilled yielded I (R = CH₂OH, A = CH₂CH₂, R' = EtO), m. 103-4°. The hydrogenation of an alc. solution of I (R = EtCO, A = CH₂CH₂, R' = PhO) in the presence of PtO₂ gave I [R = EtCH(OH), A = CH₂CH₂, R' = PhO];HBr salt, m. 178°. A mixture of 20 parts II [R = EtCH(OH) (IV)], 250 parts pentanol, 5 parts Na₂CO₃, and 20 parts IV (R' = 2-tetrahydrofuryl, A = CH₂, X = Cl), n_{20D} 1.4553, was refluxed 48 hrs., the suspension filtered, and the filtrate distilled to give I [R = EtCH(OH), A = CH₂, R' = 2-tetrahydrofuryl], b_{0.05} 170°, n_{20D} 1.5375. A similar alkylation method was used to prepare I (R = CH₂OH, A = CH₂CH₂, R' = Ph), m. 108° and I (R = CH₂OH, A = CH₂CH₂, R' = HOCH₂CH₂O), b_{0.2} 180-90°. IV, b_{0.5} 10-5°, was prepared by the PtO₂-catalyzed reduction of II (R = EtCO), b_{0.4} 135°, n_{20D} 1.5467, and II (R = CH₂OH), m. 80°, was obtained by the LiAlH₄ reduction of II (R = CO₂Et). The I were nonadditive antitussives without pethidine-like analgesic properties.

AN 1962:79391 CAPLUS

DN 56:79391

OREF 56:15490a-f

TI 4-(1-Hydroxyalkyl)-4-phenyl-1-substituted-piperidines

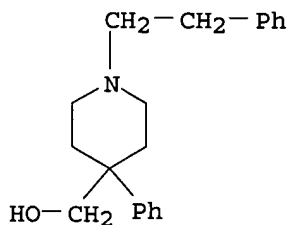
IN Stern, Edward Severin; Watt, Robert L.; Hardy, Denis G.

PA J. F. Macfarlan & Co., Ltd.

DT Patent

LA Unavailable

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 888657		19620131	GB	19580714
	US 3108111		1963	US	
IT	63080-12-6, 4-Piperidinemethanol, 1-phenethyl-4-phenyl- (preparation of)				
RN	63080-12-6 CAPLUS				
CN	4-Piperidinemethanol, 4-phenyl-1-(2-phenylethyl)- (9CI) (CA INDEX NAME)				



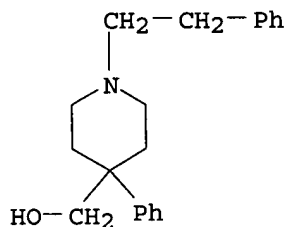
=> d abs bib hitstr 30-39

L11 ANSWER 30 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

GI

with CH₂N₂, and evidence for oxide by-products has been obtained. 4-Phenylazacycloheptan-4-ols have been made from the azacycloheptanones, and their esterification and dehydration investigated. The ethanolysis and Thorpe-Ziegler cyclization of N-(2-cyanoethyl)-N-(3-cyanopropyl)benzylamine has been studied. The cyclic product has been shown to have an enamionitrile structure.

AN 1965:29636 CAPLUS
 DN 62:29636
 OREF 62:5256a
 TI Synthesis and reactions of some azacycloheptan-4-ols
 AU Casy, A. F.; Birnbaum, H.
 CS Chelsea Coll. Sci. Technol., London
 SO Journal of the Chemical Society, Abstracts (1964), (Dec.), 5130-4
 CODEN: JCSAAZ; ISSN: 0590-9791
 DT Journal
 LA English
 OS CASREACT 62:29636
 IT 1231-52-3, 4-Piperidinemethanol, 1-phenethyl-4-phenyl-,
 hydrochloride
 (preparation of)
 RN 1231-52-3 CAPLUS
 CN 4-Piperidinemethanol, 1-phenethyl-4-phenyl-, hydrochloride (7CI, 8CI) (CA
 INDEX NAME)



● HCl

L11 ANSWER 48 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
 AB cf. CA 59, 13935e. A series of N-substituted derivs. of 4-phenyl-4-carbethoxypiperidine (I) was prepared for pharmacological testing. I (46.6 g., b_{0.5} 140°, m. 36-8°) and 42 g. K₂CO₃ in 250 ml. anhydrous C₆H₆ treated, under stirring, dropwise with 31 g. BzCH₂Cl (II) in 200 ml. C₆H₆ in 45 min. at room temperature, the mixture stirred 2 hrs., refluxed 1 hr., kept overnight at room temperature, and worked up gave 63.2 g. 1-phenacyl-4-phenyl-4-carbethoxypiperidine (III), m. 114° (C₆H₆-petr. ether or 60% EtOH); HCl salt m. 175-80° (Me₂CO-EtOH-Et₂O). III (15 g.) in 150 ml. anhydrous EtOH, Pd-C (prepared from 3 g. PdCl₂) and 0.3 g. PdCl₂ hydrogenated under shaking at normal conditions 5 hrs. gave 9.4 g. 1-(2-phenyl-2-hydroxyethyl)-4-phenyl-4-carbethoxypiperidine (IV), m. 128.5° (80° EtOH); HCl salt m. 192° (aqueous EtOH). IV (3 g.), 15 ml. anhydrous C₅H₅N, and 15 ml. Ac₂O kept overnight at room temperature and worked up gave 3.0 g. HCl salt of 1-(2-phenyl-2-acetoxyethyl)-4-phenyl-4-carbethoxypiperidine monohydrate, m. 110-20° and 173-5° (H₂O). IV (3 g.), 15 ml. anhydrous C₅H₅N, and 15 ml. (EtCO)₂O gave similarly 3.7 g. HCl salt of 1-(2-phenyl-2-

L11 ANSWER 46 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

GI For diagram(s), see printed CA Issue.

AB The title compds. I, useful as muscle relaxants, were prepared Thus 35 g. AlCl₃ was added to 200 ml. PhOPh, 35 g. γ -chlorobutyryl chloride added, and the solution stirred 1 hr. to give p-Cl(CH₂)₃COC₆H₄OPh. A mixture of 0.05 mole p-phenoxy- β -chloropropionate, 0.05 mole 4-phenyl-1,2,5,6-tetrahydropyridine, 0.05 mole Et₃N, and 25 ml. HCONMe₂ was heated at 70 for 4 hrs., poured into H₂O, worked up, and 2-naphthalenesulfonic acid in 200 ml. iso-PrOH added to give 16 g. 1-[2-(p-phenoxybenzoyl)ethyl]-4-phenyl-1,2,5,6-tetrahydropyridine 2-naphthalenesulfonate, m. 190.5-91°, which was converted to the free base (II) and then to the hydrochloride, m. 190-1°, by adding excess alc. HCl. Similarly prepared were 1-[γ -(p-phenoxybenzyl)propyl]-4-phenyl-1,2,5,6-tetrahydropyridine 2-naphthalenesulfonate, m. 202-3.5°; HCl salt, m. 163-65°. A mixture of 0.005 mole II, 0.005 mole NH₂OH.HCl, and 20 ml EtOH was heated in warm water for 2 hrs. to give II oxime, m. 182-4°. A mixture of 0.01 mole II, 0.05 mole NaBH₄, and 150 ml. EtOH was refluxed 6 hrs. to give 65% 1-[3-hydroxy-3-(p-phenoxyphenyl)propyl]-4-phenyl-1,2,5,6-tetrahydropyridine-HCl, m. 203-3.5°. Similarly prepared were 3-[N-(4-phenyl-1,2,5,6-tetrahydro-1-pyridyl)]-1-[4-(p-nitrophenoxy)phenyl]-1-propanol-HCl, m. 214-15°; N-[4-hydroxy-4-(p-phenoxyphenyl)butyl]-4-phenyl-1,2,5,6-tetrahydropyridine-HCl, m. 160-1°; 3-piperidino-1-(p-phenoxyphenyl)-1-propanol, m. 79-81°; 4-piperidino-1-(p-phenoxyphenyl)-1-butanol-HCl, m. 153-3.5° (iso-PrOH-heptane); 4-(o-methoxyphenyl-1-piperazinyl)-1-(p-phenoxyphenyl)-1-butanol-HCl, m. 199-201°; 3-[N-(4-phenyl-1,2,5,6-tetrahydro-1-pyridyl)]-1-[4-p-fluorophenoxy)-phenyl]-1-propanol, m. 112-13°. A mixture of 0.05 mole 4-(p-nitrophenoxy)acetophenone, 0.05 mole paraformaldehyde, 0.05 mole 4-phenyl-1,2,5,6-tetrahydropyridine-HCl, and 25 ml. HOAc was stirred at 95° for 2 hrs. The HOAc was evaporated and the residue diluted with acetone to give 11.68 g. 2-[4-(4-nitrophenoxy)benzoyl]ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-HCl, m. 198-9°. Similarly prepared were 1-(o-methoxyphenyl)-4-[2-(p-phenoxybenzoyl)ethyl]piperazine-HCl, m. 173-5°; 2-[4-(p-fluorophenoxy)benzoyl]ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-HCl, m. 192-3° (BuOH). A mixture of 0.005 mole 3-(4-phenyl-1,2,5,6-tetrahydro-1-pyridyl)-1-(p-phenoxyphenyl)-1-propanol, 0.005 mole BuNCO, and 30 ml. toluene was refluxed for 2 hrs., the toluene evaporated, and the residue treated with 0.6 g. fumaric acid (in iso-PrOH) to give 3-(4-phenyl-1,2,5,6-tetrahydro-1-pyridyl)-1-(phenoxyphenyl)-1-propanol N-butylcarbamate fumarate, m. 128-30° (heptane-BuOH). A solution of 0.15 mole piperidine, 0.075 mole p-phenoxy-3-chloropropiophenone, and 30 ml. HCONMe₂ was heated at 70° for 4 hrs. and the product treated with 13 g. 2-naphthalenesulfonic acid (in iso-PrOH) to give 11.5 g. β -(N-piperidino)-p-phenoxypropiofenone 2-naphthalenesulfonate, m. 140-3°. The base, m. 168-71°, was liberated from the salt and then converted into the HCl salt, m. 162-3°. A mixture of 0.075 mole piperidine, 0.075 mole γ -chloro-p-phenoxybutyrophenone, 0.075 mole anhydrous K₂CO₃, 0.075 mole NaI, 30 ml. HCONMe₂, and 6.4 g. piperidine was refluxed 24 hrs. and the product treated with 15 g. ClO₄H₇SO₃H-2 to give 8.4 g. γ -(N-piperidino)-p-phenoxybutyrophenone-ClO₄H₇SO₃H-2. Similarly prepared were 1-[γ -(p-phenoxybenzoyl) propyl]-4-hydroxypiperidine, m. 97.5-8.5° (heptane-iso-PrOH), HCl salt m. 104-6°; 1-[γ -(p-phenoxy)benzoylpropyl]-4-(m-trifluoromethylphenyl)-4-hydroxypiperidine-ClO₄H₇SO₃H-2, m. 161-3° (ios-PrOH); 1-[γ -(p-phenoxybenzoyl)-4-phenyl-4-

hydroxymethylpiperidine-C10H7SO3H-2, m. 129.5-32°;
 γ -[N-4-(carbethoxy-4-phenylpiperidino)-p-phenoxybutyrophenone]-C10-
H7SO3H-2 (number m.p. reported); 1-[γ -(p-phenoxybenzoyl)propyl]-4-(o-
methoxyphenyl)piperazine-C10H7SO3H-2, m. 215-17°; HCl salt m.
202-4°. A MeOH solution of 0.004 mole 1-(o-methoxyphenyl)-4-[2-(p-
phenoxybenzoyl)ethyl]piperazine was treated with 0.004 mole NaBH4 in 3
portions over 1.5 hrs. to give 1.35 g. 1-(o-methoxyphenyl)-4-(p-
phenoxycinnamyl)piperazine-HCl, m. 164.5-5.5°.

AN 1969:87583 CAPLUS

DN 70:87583

TI N-(p-Phenoxybenzoylalkyl)-4-phenyl-1,2,5,6-tetrahydropyridines and the
corresponding alcohols and carbamates

IN Biel, John H.; Hopps, Harvey B.

PA Aldrich Chemical Co., Inc.

SO U.S., 11 pp.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3426036	A	19690204	US 1966-570186	19660804
PRAI	US 1966-570186	A	19660804		

IT 22620-52-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

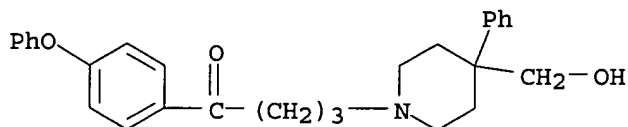
RN 22620-52-6 CAPLUS

CN 2-Naphthalenesulfonic acid, compd. with 4-[4-(hydroxymethyl)-4-
phenylpiperidino]-4'-phenoxybutyrophenone (1:1) (8CI) (CA INDEX NAME)

CM 1

CRN 47695-27-2

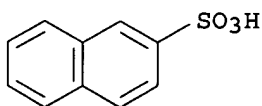
CMF C28 H31 N O3



CM 2

CRN 120-18-3

CMF C10 H8 O3 S



L11 ANSWER 47 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

AB 4-Piperidones have been ring-expanded to azacycloheptanones by reaction

propionyxyethyl)-4-phenyl-4-carbethoxypiperidine, m. 153-5°
(Me₂CO-EtOHEt₂O). I (10 g.) and 3.5 g. anhydrous C₅H₅N in 50 ml. anhydrous

C₆H₆

treated with 10 g. Ph₂CHCOCl (V) in 50 ml. C₆H₆ under stirring in 30 min., and the mixture kept overnight at room temperature and worked up gave 16.3 g. 1-(diphenylacetyl)-4-phenyl-4-carbethoxypiperidine (VI), m. 94-6° (C₆H₆-petr. ether). I (10 g.) and 10 g. phenylcyclohexylacetyl chloride (VII) gave similarly 13.5 g. 1-(phenylcyclohexylacetyl)-4-phenyl-4-carbethoxypiperidine (VIII), m. 152-3° (C₆H₆-petr. ether). VI (10 g.) reduced with 3 g. LiAlH₄ in 425 ml. anhydrous Et₂O in 5 hrs., and the mixture refluxed 3 hrs. and worked up gave 8.3 g. 1-(2,2-diphenylethyl)-4-phenyl-4-hydroxymethylpiperidine, m. 106-8° (Et₂O); HCl salt m. 219-25° (EtOH-Me₂CO). VIII (11 g.) gave similarly 8.1 g. 1-(2-phenyl-2-cyclohexylethyl)-4-phenyl-4-hydroxymethylpiperidine, m. 105-6° (anhydrous Et₂O); HCl salt m. 168-72° (Me₂COEt₂O). I (15 g.) and 6.2 g. Cl(CH₂)₂OH heated 5 hrs. at 100° and worked up gave 13.7 g. 1-(2-hydroxyethyl)-4-phenyl-4-carbethoxypiperidine, b₁ 164-74°, m. 70-80°; HCl salt m. 142-4° (EtOH-Et₂O). NaNH₂ (9 g.) in 150 ml. anhydrous C₆H₆ stirred and treated with 12 g. Ph₂C(OH)Me, the mixture stirred 20 min. at room temperature, treated with 20 g. HCl salt of 1-(2-chloroethyl)-4-phenyl-4-carbethoxypiperidine (m. 215°), refluxed 7 hrs. with stirring, cooled, decomposed with 150 ml. H₂O, the organic layer evaporated in vacuo, and the glassy residue (27.7 g.) chromatographed on 360 g. neutral Al₂O₃ gave on elution with CHCl₃ 14 g. 1-[2-(1,1-diphenylethoxy)ethyl]-4-phenyl-4-carbethoxypiperidine, m. 95-6° (C₆H₆-petr. ether); picrate m. 162° (anhydrous EtOH); methanesulfonate monohydrate m. 84-5° (C₆H₆-Et₂O-petr. ether). I (23.3 g.), 100 ml. iso-AmOH, 9.3 g. anhydrous K₂CO₃, and 30 g. Me₂N(CH₂)₃Cl refluxed 30 hrs. and worked up gave 11.6 g. 1-(3-dimethylaminopropyl)-4-phenyl-4-carbethoxypiperidine, b₁ 190°; di-HCl salt hemihydrate m. 240-1° (EtOH); dimethiodide m. 230-2° (EtOH). I (30 g.) and 50 ml. CH₂:CHCN kept overnight at room temperature, the mixture treated with

0.5

ml. 50% Et₃N(CH₂Ph)OH, heated 3 hrs. in a boiling water bath, evaporated in vacuo, and the residue distilled gave 34 g. 1-(2-cyanoethyl)-4-phenyl-4-carbethoxypiperidine (IX), b₁ 194-8°, m. 51.5° (Et₂O-petr. ether); HCl salt m. 193° (Me₂CO-EtOH). IX (8 g.) and 1.75 ml. anhydrous EtOH in 15 ml. anhydrous CHCl₃ cooled, saturated with anhydrous HCl, and the

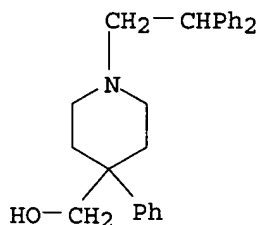
mixture kept

3

in a closed vessel 2 weeks at room temperature and worked up gave 3 g. di-HCl salt of 3-(4-phenyl-4-carbethoxypiperidino)propionamide, m. 188-90° (MeOH-Et₂O). MeONa (prepared from 1 g. Na and 10 ml. anhydrous MeOH) treated with 3 g. NH₂OH.HCl, the mixture stirred 10 min., filtered, the filtrate treated with 5.72 g. IX in 5 ml. MeOH, and the mixture kept overnight at room temperature and worked up gave 3 g. di-HCl salt of 3-(4-phenyl-4-carbethoxypiperidino) propionamidoxime, m. 172-4° (MeOH-Et₂O). I (30 g.) and 50 ml. CH₂:CHCO₂Et kept 4 hrs. at room temperature, the mixture heated 3 hrs. at 100-10°, evaporated in vacuo, and the residue distilled gave 23.5 g. 1-(2-carbethoxyethyl)-4-phenyl-4-carbethoxypiperidine, b_{0.6} 184-6°; HCl salt m. 147° (Me₂CO). I (10.8 g.) in 45 ml. anhydrous Et₂O stirred, treated with 3.5 g. CH₂:CHAc in 10 ml. Et₂O (under reflux), the mixture kept overnight and evaporated, and the residue mixed with petr. ether gave 13.5 g. 1-(3-oxobutyl)-4-phenyl-4-carbethoxypiperidine (X), m. 64.5-5.5° (petr. ether); HCl salt m. 147-50° (MeOH-Et₂O). X (5.5 g.), 5 g. NH₂OH.HCl, 50 ml. EtOH, and 5 ml. C₅H₅N refluxed 2 hrs. and worked up gave 1-(3-hydroxyiminobutyl)-4-phenyl-4-carbethoxypiperidine, m. 149-52° (EtOH); di-HCl salt m. 129-32° (MeOH-Et₂O); methiodide m. 167-9° (EtOH-Et₂O). I

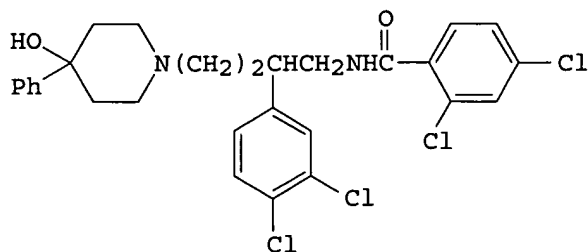
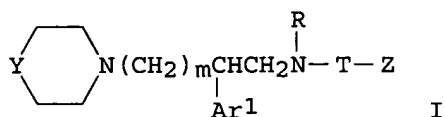
(10 g.) and 5.2 ml. concentrated HCl in 15 ml. H₂O heated to 75-80°, the solution stirred, treated dropwise in 45 min. with 3.3 g. NaNO₂ in 10 ml. H₂O, and the mixture stirred 2 hrs. at 75-80°, kept overnight at room temperature, and worked up gave 11.5 g. 1-nitroso-4-phenyl-4-carbethoxypiperidine (XI), m. 43-5° (Et₂O-petr. ether). XI (9 g.) in 100 ml. 75% AcOH stirred at 60°, treated in 1 hr. with 25 g. Zn, and the mixture stirred 2 hrs. at 60°, cooled, filtered, and the filtrate worked up gave 4.5 g. HCl salt of 1-amino-4-phenyl-4-carbethoxypiperidine, m. 173-7° (EtOH-Et₂O). The analgesic, antispasmodic, mydriatic, and central depressing activities of the products are tabulated; III is the most active of the series.

AN 1964:30816 CAPLUS
 DN 60:30816
 OREF 60:5451f-h,5452a-g
 TI Synthetic analgesics. V. Synthetic experiments based on 4-phenyl-4-carbethoxypiperidine (norpethidine)
 AU Protiva, M.; Jilek, J. O.; Pomykacek, J.; Jirkovsky, I.; Vejdelek, Z. J.
 CS Pharm. Res. Inst., Prague
 SO Collection of Czechoslovak Chemical Communications (1963), 28, 2627-36
 CODEN: CCCCAK; ISSN: 0010-0765
 DT Journal
 LA Unavailable
 IT **96072-68-3**, 4-Piperidinemethanol, 1-(2,2-diphenylethyl)-4-phenyl-, hydrochloride **96072-69-4**, 4-Piperidinemethanol, 1-(2,2-diphenylethyl)-4-phenyl- **96763-96-1**, 4-Piperidinemethanol, 1-(β-cyclohexylphenethyl)-4-phenyl-, hydrochloride **804442-77-1**, 4-Piperidinemethanol, 1-(β-cyclohexylphenethyl)-4-phenyl- (preparation of)
 RN 96072-68-3 CAPLUS
 CN 4-Piperidinemethanol, 1-(2,2-diphenylethyl)-4-phenyl-, hydrochloride (7CI) (CA INDEX NAME)



● HCl

RN 96072-69-4 CAPLUS
 CN 4-Piperidinemethanol, 1-(2,2-diphenylethyl)-4-phenyl- (7CI) (CA INDEX NAME)



AB Title compds. I [Y = Cy-N, Ar(CH₂)_xC(X); Cy = (substituted) Ph, cycloalkyl, pyrimidinyl, pyridyl; Ar = (substituted) Ph, pyridyl, thienyl; x = 0, 1; X = OH, alkoxy, hydroxyalkyl, acyloxy, phenacyloxy, CO₂H, carbalkoxy, cyano, aminoalkyl, (di)(alkyl)amino, alkanoylamino, acyl, etc.; m = 2, 3; Ar' = (substituted) Ph, (benzo)thienyl, naphthyl, (N-alkyl)indolyl; R = H, alkyl; T = CO, CONH, C(S)NH; Z = H, M, OM; M = alkyl, (substituted) phenylalkyl, pyridylalkyl, (substituted) naphthylalkyl, pyridylthioalkyl, styryl, etc.] were prepared for use as antiasthmatics and bronchodilators. For example, N-[2-(3,4-dichlorophenyl)-4-hydroxybutyl]-2,4-dichlorobenzamide (preparation given) was converted to the mesylate ester by MeSO₂Cl, followed by amination with 4-hydroxy-4-phenylpiperidine, chromatog., and salification, to give title compound II as the HCl salt. I displaced [2-¹²⁵I histidyl]-neurokinin A from NK-2 receptors of rat duodenal membranes with K_i = 0.50-3 nM, and antagonized NK-2 agonist-induced bronchospasm in guinea pigs.

AN 1992:426590 CAPLUS

DN 117:26590

TI Piperidine- and piperazine-containing arylalkylamines, process for their preparation, and pharmaceutical compositions containing them as neurokinin receptor antagonists.

IN Emonds-Alt, Xavier; Goulaouic, Pierre; Proietto, Vincenzo; Van Broeck, Didier

PA Sanofi SA, Fr.

SO Eur. Pat. Appl., 54 pp.

CODEN: EPXXDW

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 474561	A1	19920311	EP 1991-402382	19910905
	EP 474561	B1	19981209		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	FR 2666335	A1	19920306	FR 1990-11039	19900905
	FR 2666335	B1	19921211		
	FR 2678267	A1	19921231	FR 1991-7824	19910625
	FR 2678267	B1	19940204		
	IL 99320	A1	19950731	IL 1991-99320	19910827
	AU 9183542	A1	19920312	AU 1991-83542	19910903
	AU 657272	B2	19950309		
	BR 9103802	A	19920519	BR 1991-3802	19910903
	CA 2050639	AA	19920306	CA 1991-2050639	19910904

CA 2050639	C	19971202		
FI 9104174	A	19920306	FI 1991-4174	19910904
FI 98457	B	19970314		
FI 98457	C	19970625		
NO 9103469	A	19920306	NO 1991-3469	19910904
NO 177226	B	19950502		
NO 177226	C	19950809		
HU 59098	A2	19920428	HU 1991-2863	19910904
ZA 9107017	A	19921230	ZA 1991-7017	19910904
PL 167994	B1	19951230	PL 1991-291618	19910904
RU 2070196	C1	19961210	RU 1991-5001435	19910904
JP 04261155	A2	19920917	JP 1991-254730	19910905
US 5236921	A	19930817	US 1991-755454	19910905
AT 174332	E	19981215	AT 1991-402382	19910905
ES 2127722	T3	19990501	ES 1991-402382	19910905
CZ 285994	B6	19991215	CZ 1991-2724	19910905
LV 10606	B	19960420	LV 1993-139	19930225
LT 3442	B	19951025	LT 1993-585	19930531
US 5350852	A	19940927	US 1993-105677	19930813
HK 1005290	A1	20000818	HK 1998-104394	19980521
PRAI FR 1990-11039	A	19900905		
FR 1991-7824	A	19910625		
US 1991-755454	A3	19910905		

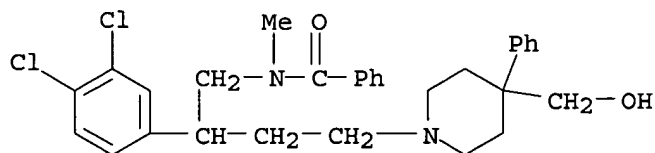
OS MARPAT 117:26590

IT 142001-40-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of, as neurokinin receptor antagonist)

RN 142001-40-9 CAPLUS

CN Benzamide, N-[2-(3,4-dichlorophenyl)-4-[4-(hydroxymethyl)-4-phenyl-1-piperidiny]butyl]-N-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L11 ANSWER 31 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

GI For diagram(s), see printed CA Issue.

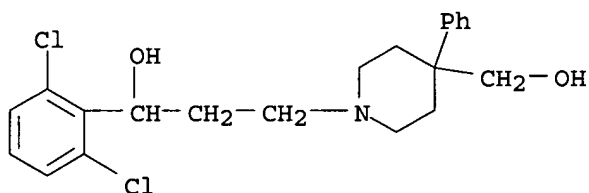
AB The title compds. I [R = dichlorophenyl, nitrocyclohexylphenyl; X = CH:NCH:CH, CH₂CH₂N(C₆H₄OMe-o)CH₂CH₂, CH₂CH₂CR₁R₂CH₂CH₂ where R₁ = H, Ph, 2-chlorophenyl, 3-pyrridyl, R₂ = H, CH₂OH, CO₂Et, CONH₂, etc.; X₁ = CO, CHOH, O] were prepared. Thus, a mixture of 14.1 g 4-(hydroxymethyl)-4-phenylpiperidine HCl, 46.8 g 2,6-dichloroacetophenone (II), 2.75 g paraformaldehyde, and 60 mL EtOH containing 0.5 mL concentrated HCl was refluxed for

24 h., 23.5 g II and 2.75 g formaldehyde were added, and the resulting mixture was refluxed for 89 h to give 6.00 g I [R = 2,6-Cl₂C₆H₃, X = CH₂CH₂CPh(CH₂OH)CH₂CH₂, X₁=CO] HCl. I had antifungal activity at 1.5625 µg/mL concentration and analgesic activity at 32-500 mg/kg in mice.

AN 1984:591709 CAPLUS

DN 101:191709
 TI 1-(2,6-Dichlorobenzoyl)ethyl)-4-(hydroxymethyl)-4-phenylpiperidine and its
 analogs
 PA Fujisawa Pharmaceutical Co., Ltd., Japan
 SO Jpn. Kokai Tokkyo Koho, 11 pp.
 CODEN: JKXXAF
 DT Patent
 LA Japanese
 FAN.CNT 1

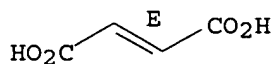
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 59106460	A2	19840620	JP 1982-217335	19821210
PRAI	JP 1982-217335		19821210		
IT	92823-90-0P 92878-25-6P				
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (preparation and biol. activities of)				
RN	92823-90-0 CAPLUS				
CN	1-Piperidinepropanol, α -(2,6-dichlorophenyl)-4-(hydroxymethyl)-4-phenyl-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)				
CM	1				
CRN	92823-89-7				
CMF	C21 H25 Cl2 N O2				



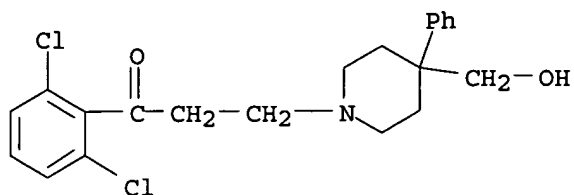
CM 2

CRN 110-17-8
 CMF C4 H4 O4

Double bond geometry as shown.

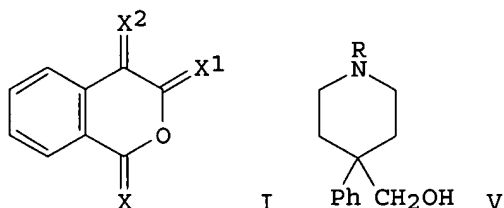


RN 92878-25-6 CAPLUS
 CN 1-Propanone, 1-(2,6-dichlorophenyl)-3-[4-(hydroxymethyl)-4-phenyl-1-piperidinyl]-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L11 ANSWER 32 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
GI



AB Spiro[isochroman-3,4'-piperidin]-1-ones I [X = O, X1 = CH₂CH₂NRCH₂CH₂, X₂ = H₂ (II); X = O, X1 = H₂, X₂ = CH₂CH₂NRCH₂CH₂ (III); (X = X1 = H₂, X₂ = CH₂CH₂NRCH₂CH₂ (IV) (R = Me, PhCH₂, PhCH₂CH₂)] were prepared, e.g. from V, and their analgesic activities were determined III, IV and V had analgesic activity at potent as aminopyrine, whereas II were inactive. Several of the compds. inhibited the histamine release induced by compound 48/80 from isolated rat peritoneal mast cells.

AN 1981:192086 CAPLUS

DN 94:192086

TI Synthesis and biological activity of spiro[isocoumarin-piperidines] and related compounds. I

AU Yamato, Masatoshi; Hashigaki, Kuniko; Ikeda, Masao; Ohtake, Hidetoshi; Tasaka, Kenji

CS Fac. Pharm. Sci., Okayama Univ., Okayama, 700, Japan

SO Chemical & Pharmaceutical Bulletin (1981), 29(2), 402-5

CODEN: CPBTAL; ISSN: 0009-2363

DT Journal

LA English

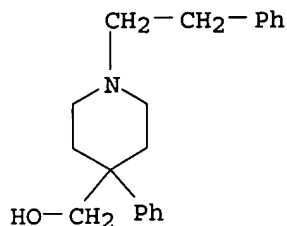
OS CASREACT 94:192086

IT 63080-12-6

RL: RCT (Reactant); RACT (Reactant or reagent)
(analgesic and antihistaminic activities of)

RN 63080-12-6 CAPLUS

CN 4-Piperidinemethanol, 4-phenyl-1-(2-phenylethyl)- (9CI) (CA INDEX NAME)

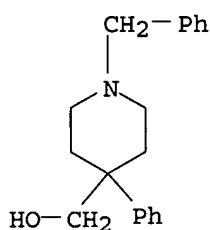


IT 59083-36-2

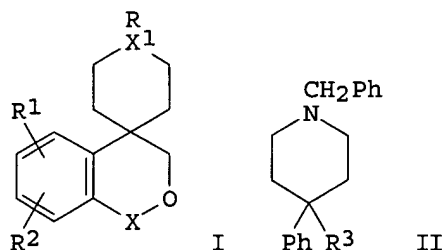
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation reaction of, with paraformaldehyde)

RN 59083-36-2 CAPLUS

CN 4-Piperidinemethanol, 4-phenyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



L11 ANSWER 33 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
GI



AB Spiroisochromans I (R = H, alkyl, aralkyl; R1, R2 = H, alkoxy, hydroxyalkyl; X = CH2, CO; X1 = N, CH) were prepared. Thus, methanolysis of 5.5 g II (R3 = CN) gave 3.3 g II (R3 = CO2Me), which was reduced quant. to II (R3 = CH2OH). Treating 4 g II (R3 = CH2OH) with (CH2O)_n, followed by HCl gave 2.1 g I.HCl (R = benzyl, R1 = R2 = H, X = CH2, X1 = N). The latter compound showed 50% inhibition of histamine release in rats at 6.7 + 10⁻⁴ mol/L in vitro.

AN 1981:121329 CAPLUS

DN 94:121329

TI Spiroisochroman

PA Daiichi Seiyaku Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 4 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 55139381	A2	19801031	JP 1979-45167	19790413
	JP 63006549	B4	19880210		
PRAI	JP 1979-45167	A	19790413		

OS CASREACT 94:121329

IT 59083-36-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and cyclocondensation of, with paraformaldehyde)

RN 59083-36-2 CAPLUS

CN 4-Piperidinemethanol, 4-phenyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)

